

Effect of Silica Nanoparticles on Rheological Properties and Gelation Temperature of Biodegradable Polymer Gels

Vivian Florián-Algarín and Aldo Acevedo

Department of Chemical Engineering, University of Puerto Rico, Mayagüez,
PO Box 9046, Mayagüez, PR 00680, contact email: aldacevedo@uprm.edu

ABSTRACT

The discovery of new potent and insoluble drugs has emphasized the need for personalized dosages and novel drug-delivery systems. The use of biodegradable polymers is a good alternative to form films in which a solid active pharmaceutical ingredient is suspended. In the processing of films, the rheology and gelation of biodegradable polymers are of particular interest. This work presents the rheological study and gelation kinetics of solid nanoparticle dispersions in aqueous gelatin solutions. Silica nanoparticles were used as surrogate particles in this study. Silica dispersions of up to 5.0 wt% in the specified biopolymer were prepared from a commercial LUDOX silica dispersion. The thermotropic gelation (T_{gel}) was experimentally determined by rheological measurements on a Reologica StressTech HR stress controlled rheometer. Particle loadings below 0.5 wt% did not have an effect on the thermotropic gelation temperature of a 10 wt% gelatin solution.

Keywords: gelatin, rheology, thermotropic gelation

1 INTRODUCTION

Biodegradable polymer gels have a variety of applications in agriculture [1], food [2], and pharmaceutical industries [3, 4]. Natural biopolymers are ideal for these applications since they are biodegradable and biocompatible. Some examples of natural biopolymers are: polysaccharides, such as starch, cellulose, lignin, and chitin; proteins, such as gelatin, casein, wheat gluten, silk, and wool; and lipids, such as plant oils, including castor oil and animal fats [5]. Biopolymers are ideal candidates as main structural agents, due to their gelling capacity, immobilization capacity in the gel network and inherent flexible processing through existing manufacturing technologies perfected in other industries. The inherent thermal processability and the thermotropy of some of these gels allow for control and flexibility during continuous processing. In recent years, inclusion of nanoparticles into a gel matrix has generated interest since it may allow for the development of novel drug and nutrient delivery systems. Nevertheless, particle size and concentration may affect network formation.

Addition of particles increase the effective viscosity of a solution as predicted by Einstein's law of viscosity and widely demonstrated experimentally. Nevertheless, the effect of colloidal particles on the physical gelation has not been systematically studied. In this work, the effect of colloidal spherical nano-silica on the gelation temperature of a gelatin solution is determined through rheological measurements.

Gelatin is one of the most common biopolymers used today. It is prepared by the thermal denaturation of collagen, isolated from animal or fish skin and bones [6, 7]. When a gelatin solution is cooled, the protein coils start to form triple helices and progressively a three-dimensional network is formed. That transition temperature is called gelation temperature (T_{gel}). This transition is thermoreversible, when it is heated it melts (i.e. transition helix to coil) [8]. T_{gel} is widely used to characterize biopolymers that form thermo-reversible gels. Gelation temperatures are affected by the biosource [8], concentration [9, 10], and cooling rate [11], amongst many others.

2 EXPERIMENTAL METHODS

2.1 Materials

Type B gelatin (batch #035K00011) and LUDOX TM-50, 50 wt% aqueous colloidal silica dispersion, were purchased from Sigma-Aldrich. The hydrodynamic diameter of the silica particles was determined as 13.1 nm with a polydispersity of 0.234 by dynamic light scattering on a Brookhaven Instruments BI 90-Plus particle size analyzer. The silica dispersion was diluted to the desired concentration in deionized water. The appropriate amount of gelatin was added and it was heated on a hot-plate at 50 °C, while stirring constantly for at least 30 minutes. No adjustments of pH were made.

2.2 Rheology and Transition Temperatures

Rheological measurements are well established methods used to determine thermal sol-gel transitions. [11-13] The method used in this report to determine the gelation temperature was the oscillatory dynamic test, where the linear viscoelastic moduli are continuously measured at a constant strain and frequency while the sample is cooled

[12, 13]. Van Den Bulcke and coworkers [13] and Ding and collaborators [11] have reported using this method to determine the temperature of gelation, and gelatin and pullulan mixtures, respectively, at different concentrations in a temperature range from 60 to 20 °C.

The gelation temperature was identified as the temperature at which the storage and loss modulus are equal (i.e. solid- and liquid-like contributions are equal) during a cooling cycle. Furthermore, upon heating an additional crossover of the moduli can be determined, which was denominated as the melting temperature. The observation of both transitions demonstrates the thermoreversible nature of the aqueous biopolymer solutions. A hysteresis between the gelling and melting temperatures is commonly observed in gelatin [6] and similar systems, such as agarose [14].

Rheological characterization was performed on either a Reologica StressTech HR stress-controlled rheometer equipped with an extended temperature cell (ETC) for temperature control using stainless steel cone-and-plate ($d = 30$ mm and $\theta < 4^\circ$) and double-gap Couette ($V = 11$ mL) fixtures, or on an Anton-Paar Physica MCR301 equipped with a Julabo constant temperature water bath control using stainless steel cone-and-plate ($d = 50$ mm and $\theta = 0.976^\circ$) The rheometer fixture was pre-heated to the desired temperature, before transferring and loading the hot solution. The sample and fixture temperature was allowed to equilibrate for at least 20 minutes. After temperature reached equilibrium, rheological tests were performed. The dynamic viscoelastic moduli were measured at a frequency of 1 Hz and a strain of 1% to guarantee measurements in the linear viscoelastic regime. The temperature was decreased from 40 to either 20 or 15 °C at a cooling rate of 2 °C/min, immediately followed by a heating cycle in the same range and at the same rate.

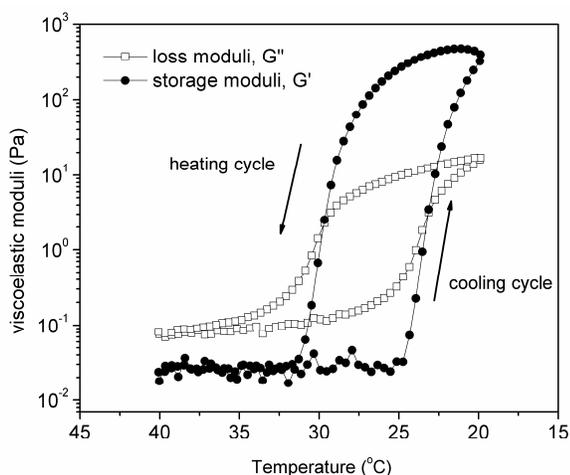


Figure 1: Dynamic viscoelastic moduli as a function of temperature for a 10 wt% aqueous gelatin solution. Cooling rate: 2 °C/min.

3 RESULTS AND DISCUSSION

Gelation temperature for gelatin solution at 10 wt% was previously measured using the constant-stress temperature ramp method at constant cooling rates (2 °C/min) and stress of 1 Pa. The gelation temperature was identified as 21.5 °C. In this work, the dynamic viscoelastic moduli method was used, as shown in Figure 1, at the same cooling rate. In this case, the transition was identified as 22.3 °C. These values are the same within experimental error, usually $\pm 15\%$.

Figure 2 shows the dynamic response when a 0.3 wt% of silica is dispersed on the gelatin solutions. In the cooling cycle, the storage moduli, G' , showed significant scattering due to the low viscosity and the Newtonian behavior of gelatin at high temperature. Neither gelation nor melting temperature was affected by the presence of the silica particles. In fact, no significant effect was observed for loadings up to 0.5 wt% as summarized in Figure 3. Thus, low concentration of silica do not perturb the formation of helical structures. A gelation temperature close to room temperature, 23.6 ± 1.1 °C was observed within this range. Melting temperature was 6.3 ± 0.2 °C above T_{gel} .

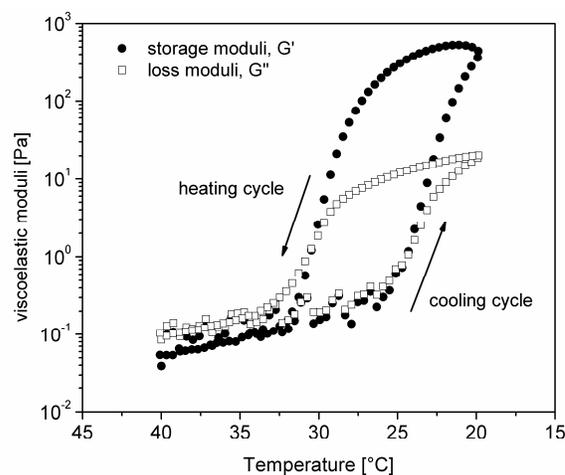


Figure 2: Dynamic viscoelastic moduli as a function of temperature for a 0.3 wt% silica dispersion in a 10 wt% aqueous gelatin solution. Cooling rate: 2 °C/min.

Nevertheless, at higher particle loadings, the gelation temperature was observed to increase with silica loadings. Thus, addition of silica particles has a positive effect on the gelation transition. Figure 4 shows the results for a 3.0 wt% silica in gelatin dispersion. In this case, gelation temperature was measured as 28.5 °C, at least six degrees higher than for the gelatin solution without silica at the same conditions. The melting point was outside the experimental window. Nevertheless, the hysteresis in the transition temperatures, if present in this sample, would be greater than 12 °C, more than double of the observed at lower loadings.

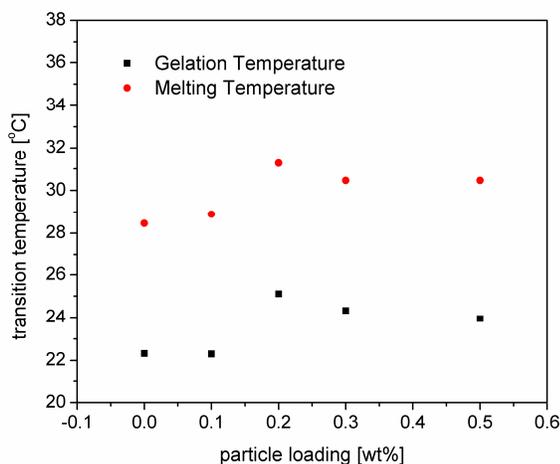


Figure 3: Effect of nano-silica loading on the gelation and melting temperatures of a 10 wt% aqueous gelatin solution.

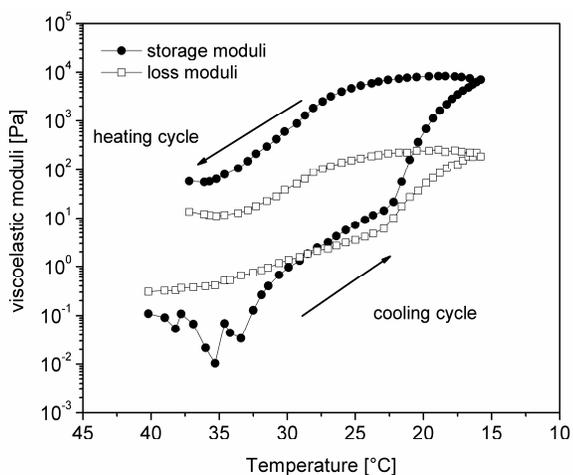


Figure 4: Dynamic viscoelastic moduli as a function of temperature for a 3.0 wt% silica dispersion in a 10 wt% aqueous gelatin solution. Cooling rate: 2 °C/min.

The positive deviation on the gelation temperature caused by high concentration of silica particles may be associated with a synergistic effect on the network formation. It is possible that the silica particles are acting as additional nodes for the network. This may have been caused by a loss of the stabilizing layer since pH was not adjusted in our experiments. Future work will consider the contribution of pH as well as expanding the concentration range.

4 ACKNOWLEDGEMENTS

The authors gratefully acknowledge the National Science Foundation (Grant 0540855) for support of this research conducted through the Engineering Research Center for Structured Organic Particulate Systems (C-SOPS) at the University of Puerto Rico at Mayagüez. The

authors thank the Rinaldi research group for the DLS results.

REFERENCES

- Russo, R., M. Malinconico, and P. Romano, *Physical behavior of biodegradable alginate-poly(vinyl alcohol) blend films*. Journal of Polymer Science Part B: Polymer Physics, 2005. **43**(10): p. 1205-1213.
- Avella, M., et al., *Biodegradable starch/clay nanocomposite films for food packaging applications*. Food Chemistry, 2005. **93**(3): p. 467-474.
- Aminabhavi, T.M., et al., *Rheological properties and drug release characteristics of pH-responsive hydrogels*. Journal of Applied Polymer Science, 2004. **94**(5): p. 2057-2064.
- Pinto, C., A. Ronald, and F. Veiga, *Alginate microparticles as novel carrier for oral insulin delivery*. Biotechnology and Bioengineering, 2007. **96**(5): p. 977-989.
- Smith, R., *Biodegradable Polymers for Industrial Applications* ed. C. Press. May 2005.
- Schrieber, R. and H. Gareis, *Gelatine Handbook: Theory and Industrial Practice*. 2007, Weinheim: Wiley-VCH Verlag GmbH & Co.
- Gómez-Guillén, M.C., et al., *Edible films made from tuna-fish gelatin with antioxidant extracts of two different murta ecotypes leaves (Ugni molinae Turcz)* Food Hydrocolloids, 2007. **21**(7): p. 1133-1143.
- Joly-Duhamel, C., D. Hellio, and M. Djabourov, *All Gelatin Networks: I. Biodiversity and Physical Chemistry*. Langmuir 2002. **18**: p. 7208-7217.
- Susan, M.T. and G.M. Alejandro, *Determination of the maximum gelation temperature in gelatin gels*. Applied Physics Letters, 2004. **84**(21): p. 4242-4244.
- Florián-Algarín, V. and A. Acevedo-Rullán, *Rheology and Gelation Temperature of Aqueous Gelatin and Sodium Alginate Solutions*. AIP Conference Proceedings, 2008. **1027**(1): p. 618-621.
- Ding, P., et al., *The effect of temperature and composition on the interfacial tension and rheology of separated phases in gelatin/pullulan mixtures*. Food Hydrocolloids, 2005. **19**(3): p. 567-574.
- Cho, J.Y., et al., *Chitosan and glycerophosphate concentration dependence of solution behavior and gel point using small amplitude oscillatory rheometry*. Food Hydrocolloids, 2006. **20**(6): p. 936-945.
- Van den Bulcke, A.I., et al., *Structural and rheological properties of methacrylamide modified gelatin hydrogels*. Biomacromolecules, 2000. **1**(1): p. 31-38.
- Fernandez, E., et al., *Rheological and thermal properties of agarose aqueous solutions and hydrogels*. Journal of Polymer Science Part B: Polymer Physics, 2008. **46**(3): p. 322-328.